Int. J. Cancer: 33, 569-576 (1984)

PATTERNS OF LUNG CANCER RISK ACCORDING TO TYPE OF CIGARETTE SMOKED

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A case-control study of lung cancer involving interviews with 7,804 cases and 15,207 hospital-based controls was carried out in seven locations in Western Europe. The large study size permitted the calculation of precise estimates of the relative risk of lung cancer associated with smoking different types of cigarettes. Lifelong nonfilter smokers were at nearly twice the risk of lung cancer compared to lifelong filter smokers after controlling for duration of cigarette use and number smoked per day (RR = 1.7 for males and 2.0 for females). Lung cancer risks for filter, nonfilter and mixed smokers increased in proportion to intensity and duration of smoking and decreased with years since stopping smoking. The findings indicate that prevention activities should continue to emphasize smoking cessation, although switching to low-tar cigarettes may also yield some reductions in lung cancer risk.

In recent years several studies have suggested that the risk of lung cancer among smokers of filter (or low-tar) cigarettes is lower than the risk for users of nonfilter (or high-tar) cigarettes (Bross and Gibson, 1968; Dean *et al.*, 1977; Hammond *et al.*, 1976; Hawthorne and Fry, 1978; Kunze and Vutuc, 1980; Reid, 1966; Rimington, 1981; Vutuc and Kunze, 1980; Wynder *et al.*, 1970; Wynder and Stellman, 1979). Small numbers of cases in these studies, especially among lifetime filter smokers and among females, have often precluded a detailed evaluation of the risk reduction associated with filter cigarettes, or of the relationships between cigarette type and other measures of cigarette exposure. This paper presents results from a case-control study involving over 23,000 subjects, focusing on the differences in risk associated with nonfilter and filter cigarettes (and high vs. low-tar) and the comparative importance of intensity, duration and cessation of smoking each type of cigarette.

MATERIAL AND METHODS

During 1976-1980 lung cancer cases were drawn from hospitals at seven study centers in Western Europe (Table I). (Data collection in Rome was initiated 1 year later in 1977 and continued through 1980.) Although the types of hospital varied, all 6,920 male and 884 female cases were ascertained from admission records or through inquiries addressed to hospital staff. Upon notification of a suspected lung cancer patient, interviews were undertaken within the shortest possible time. Nearly all patients agreed to be interviewed. If the diagnosis was verified as primary lung cancer, the subject was retained as a case. In the rare instances when a subject was discharged from hospital prior to interview, no attempt was made to follow-up and the individual was omitted from the study.

Two controls were matched to each case by sex, age and study site. Controls were obtained by searching records of the various hospital units, then interviewed, usually a few weeks after the case. At several study sites matching was also carried out on hospital accommodation. For other sites this criterion was impractical, since accommodation was not related to socioeconomic status but to the physical condition or the medical treatment of the patient. Two controls could not be obtained for all cases, so that not all matched triples were complete.

During the first 6-12 months of the study, controls were accepted if they had no present or previous tobacco-related diseases. (Unacceptable control diseases included: cancers of the oropharynx, larynx, esophagus, pancreas, liver, kidney and bladder, myocardial infarction, stroke, peripheral vascular disease, aortic aneurysm, chronic bronchitis, emphysema, peptic ulcer, cirrhosis of liver, arteriosclerosis and other vascular diseases. This list was modified in 1977; see footnote to Table II). Because of the difficulty in locating suitable controls and their obviously reduced tobacco exposure, this criterion was changed in all areas except France, thus permitting patients currently admitted for a disease not considered to be tobacco-related to serve as controls. The change in the control selection criteria had a negligible impact on results because of the large study size and the small number enrolled during the start-up phase. In almost all areas controls also were matched to the case by hospital. However, because of the different health care delivery systems, with some hospitals being specialized oncology or pulmonary centers, some controls were recruited from nearby hospitals or clinics. In all, 13,460 male and 1,747 female controls were enrolled. The distribution of the control diseases is given in Table II.

All subjects were interviewed by trained interviewers using a precoded questionnaire. Due to design constraints (specialized hospitals, or cancer wards or floors) not all interviewers could be blinded to the

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Received: November 30, 1983 and in revised form February 29, 1984.

TABLE I – SIZE OF STUDY POPULATION AND SOME CHARACTERISTICS OF ACQUISITION

Country	Sex	Cases	Controls	Characteristics of acquisition
Austria	M F	1,580 250	3,160 500	Subjects from nine hospitals located throughout the country. Some controls selected from the practice of the referring physicians where most were undergoing general health examination
France	M F	1,529 96	2,899 192	Subjects from 16 hospitals, 13 within the metropolitan area of Paris. Persons who had immigrated within the previous 10 years were excluded
Germany	M F	392 70	721 133	Hamburg: Cases and controls obtained from two hospitals
	M F	506 52	961 92	Heidelberg: Cases from a specialized hospital and controls from a nearby hospital or from among visitors to the hospital
Italy	M F	1,115 87	2,123 172	Milan: For initial 3 years subjects from five Milan area hospitals (approx. half of all lung cancers). Afterwards study transferred to Varese Province, adjacent to Milan, where a registry was utilized to obtain nearly all incident cases
	M F	1,141 103	2,282 206	Rome: subjects from nine largest hospitals. Data collection initiated 1 year after other sites
Scotland	M F	657 226	1,314 452	Study covered all 11 major hospitals in Glasgow and surrounding areas
Total	M F	6,920 884	13,460 1,747	2063630371

subjects' status. However, because of the size and the multicentral nature of this study, quality control and interviewer comparability were emphasized continually. Interviewers were closely supervised and most worked for the duration of the data collection; the turnover rate was very low.

TABLE II – DISTRIBUTION OF CONTROLS BY DIAGNOSTIC CATEGORY

Disease category	Male	Female
Cancer of stomach	226	19
Cancer of colon/rectum	476	52
Cancer of prostate	150	0
Cancer of kidney[1]	32	1
Cancer of breast	22	167
Cancer of cervix	0	53
Cancer of skin, melanoma, basal-cell carcinoma	252	15
Leukemias	68	3
Lymphomas, Hodgkin's disease	253	38
Sarcomas	89	14
Other cancers (site specified)	432	94
Benign neoplastic disease, fibrocystic lesion	1,062	72
Fractures	897	77
Tuberculosis	1,092	86
Infective or parasitic disease	851	105
Diabetes mellitus	455	46
Anemia	106	29
Appendicitis, intestinal obstruction and hernia	633	59
Pancreatitis	96	4
Nephritis and nephrosis	201	25
Motor vehicle accidents	266	10
Myocardial infarction[1]	69	5
Gastric ulcer[1]	86	3
Acute bronchitis	198	18
Nutritional and metabolic diseases	284	36
Chronic rheumatic heart disease	108	19
Hypertensive disease	306	50
Arteriosclerosis and other vascular diseases	248	23
Arthritis	48	9
GB and biliary duct disease and inflammation	469	102
Cirrhosis of liver[1]	105	4
Other non-neoplastic disease	3,880	509
Totals	13,460	1,747

[1] Control diseases acceptable until December 1977, and unacceptable after this date.

For each sex, analyses were based on estimates of relative risk (RR) within strata defined by study center and, where appropriate, by other factors. Summary RRs across strata and confidence intervals (CI) were obtained by the conditional likelihood method of Gart (1970). All RRs given in the Tables were adjusted at least for center. Tests for linear trend for variables with multiple exposure levels utilized the Mantel extension procedure (Mantel, 1963) with consecutive integers defining the ordered categories. For the tests of trend, *p*-values reflect one-sided probabilities. Additional analyses were carried out based on multivariate regression methods for matched data (Breslow *et al.*, 1978; Lubin, 1981); results closely paralleled the unmatched (stratified) analyses.

This paper focuses on the lung cancer association with filter and nonfilter cigarette use. Other analyses of risk patterns by cigar/pipe use, histologic typs and cessation of cigarette use are in preparation.

RESULTS

Table III shows that the ages at interview for controls were similar to those of cases, with the age distribution being similar for male and female cases. Cases had completed slightly fewer years of schooling and were less often ward patients. Only slight differences were observed by martial status, with males more likely to be married and females to be widowed.

The vast majority of respondents were cigarette smokers exclusively or had never smoked on a regular bases (Table IV). A total of 2.8% of the male cases and 19.4% of their controls never smoked, while for females the corresponding figures were 37.7% and 67.5%. Among males there was a 9.0-fold excess risk

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TABLE III – DISTRIBUTION OF RESPONDENTS BY DEMOGRAPHIC CHARACTERISTICS

	Males		Females	
	Cases	Controls	Cases	Controls
Total number	6,920	13,460	844	1,747
Age at interview	%	%	%	%
<50	11	15	14	15
50-59	33	34	29	31
60-69	36	32	37	34
70+	19	20	21	21
Mean age	60.8	60.2	60.7	60.6
Years of schooling	%	%	%	%
0-8	55	50	41	41
9-12	34	33	54	47
13+	11	17	7	12
Mean years	8.0	8.5	8.5	8.6
Hospital status	%	%	%	%
Private	6	6	9	7
Semi-private	60	57	55	54
Ward	30	34	34	39
Out-patient	4	3	2	1
Material status				
Single	6	7	10	10
Married	83	80	57	62
Divorced	3	4	7	4
Separated	1	1	1	0
Widowed	7	8	26	24

of lung cancer with cigarette use, a slightly lower excess for cigarette and pipe (RR = 8.1) or cigar (RR = 6.9) use and an even smaller excess with exclusive pipe (RR = 2.5) or cigar (RR = 2.9) use. Among females, almost all smokers used cigarettes exclusively and were at a 3.9-fold excess risk. Subjects smoking pipes and/or cigars exclusively were omitted from the following analyses.

Data were obtained on smoking duration, number smoked per day and names of the four previous brands smoked. A large majority (62.5%) smoked one or two brands, while 87.1% consumed three or fewer; the remainder smoked four or more brands. When more than four brands were reported during the interview, most often consecutive brands were combined. Less frequently, if the smoker switched brands numerous times within a short period of time, years of use were summed and the cigarette brand was coded as mixed, or the four brands of longest duration were used. The coding procedure varied slightly by study site.

Filter vs. nonfilter users

On the basis of all brands smoked, subjects were categorized as lifetime filter, lifetime nonfilter or mixed users. The risk of lung cancer was higher among exclusive nonfilter smokers and mixed smokers than among lifetime filter smokers, after adjusting for cessation and either years of use or number per day (Table V). After adjusting simultaneously for years of use, number smoked per day, and years since cessation, smoking nonfilter cigarettes exclusively (or mixed brands) resulted in 1.7-fold (1.6-fold) excess risks for males and 2.0-fold (1.7-fold) excess risks for females compared to smoking filter brands exclusively.

Table V also shows RRs associated with duration and intensity of smoking each cigarette type, adjusting for time since cessation of cigarette use, since current smokers were more likely to be mixed or lifelong filter users. Among males the risks of lung cancer increased with years of use for all cigarette types, with the gradients not significantly different by type. There was more variability among females (where numbers were smaller): the risks increased with duration for filter and mixed smokers, but were variable for nonfilter smokers. Based on regression models, the gradients of increase with duration were only slightly greater in males than in females (but the differences by sex were statistically significant, $p<0.01$). The RRs also increased with number smoked per day for each cigarette type, but the gradients of increase for each sex were not significantly different by type.

For each type of smoker, RRs were cross-classified by duration and number per day (Table VI). Results are shown only for males, as data were insufficient for females. Among filter, mixed and nonfilter smokers, the risks increased with duration of smoking and number of cigarettes smoked per day within all categories of the other variable, thus suggesting separate effects. Based on a regression model for matched data, these variables (duration and number per day) combined in a fashion consistent with a multiplicative effect upon cancer risk.

Table VII shows RRs of lung cancer according to the proportion of time that nonfilter cigarettes were smoked (*i.e.*, years of smoking nonfilter cigarettes divided by total years of smoking). After adjustment for years of cigarette use, number smoked per day and years since cessation, there was a marked increase in risk among those who used nonfilter cigarettes, but only a small gradient among the mixed smokers with

TABLE IV – RELATIVE RISK OF LUNG CANCER BY TYPE OF TOBACCO PRODUCT USED

Type of tobacco product	Males			Females		
	Cases	Controls	RR	Cases	Controls	RR
Never smoked	3%	19%	1.0	38%	68%	1.0
Cigarettes only	87%	69%	9.0**	62%	32%	3.9*
Cigarettes and cigars	3%	3%	6.9**	0.1%	0.1%	3.3
Cigarettes and pipes	5%	4%	8.1**	0.1%	0%	—
Cigars only	1%	1%	2.9**	0%	0%	—
Cigars and pipes	0.3%	1%	4.6**	0%	0%	—
Pipes only	1%	2%	2.5**	0%	0%	—
Cigarettes, cigars and pipes	1%	1%	7.5**	0%	0%	—
Total number	6,919	13,458		884	1,747	

*$p<0.05$; **$p<0.001$.

TABLE V – TRENDS IN RELATIVE RISK OF LUNG CANCER BY YEARS OF USE FOR LIFETIME FILTER, LIFETIME NONFILTER AND MIXED CIGARETTES SMOKERS. ALL RISKS ADJUSTED FOR YEARS SINCE CESSATION

	Males								
	Filter		Mixed		Nonfilter		Relative risks		
	Cases	Controls	Cases	Controls	Cases	Controls	Filter	Mixed	Nonfilter
Total No.	326	851	4,563	6,595	1,737	2,988			
Years of use									
1-29	37%	60%	11%	20%	19%	39%	1.0[1,2]	2.0[2]	2.5[2]
30-39	40%	27%	33%	36%	34%	29%	2.3	2.8	3.5
40-49	16%	9%	33%	28%	30%	21%	2.9	3.5	4.2
50+	8%	4%	22%	17%	17%	11%	2.8	3.6	3.7
Adjusted							1.0	1.6	1.8
95% CI								1.3-1.8	1.5-2.1
Number per day									
1-9	6%	17%	39%	48%	5%	15%	1.0[1,2]	3.2[2]	1.4[2]
10-19	26%	35%	21%	23%	28%	32%	2.0	3.7	4.6
20-29	36%	32%	26%	20%	38%	32%	2.6	5.9	5.5
30+	31%	16%	14%	10%	30%	20%	5.8	7.7	8.1
Adjusted							1.0	2.1	2.1
95% CI								1.8-2.4	1.8-2.5
	Females								
Total No.	102	184	393	330	56	53			
Years of use									
1-29	57%	65%	15%	26%	27%	47%	1.0[1,2]	1.8[2]	4.5[2]
30-39	28%	24%	36%	39%	30%	25%	1.5	2.6	4.1
40-49	10%	8%	33%	29%	27%	15%	1.5	3.0	6.9
50+	5%	3%	17%	6%	16%	13%	1.7	7.3	2.7
Adjusted							1.0	1.8	2.5
95% CI								1.3-2.6	1.2-5.2
Number per day									
1-9	19%	35%	32%	43%	11%	23%	1.0[1,2]	2.8[2]	1.6[2]
10-19	55%	39%	37%	36%	36%	42%	4.1	6.4	10.4
20-29	19%	17%	24%	17%	38%	30%	2.7	11.5	12.4
30+	8%	9%	7%	4%	16%	6%	2.8	26.3	34.7
Adjusted							1.0	2.3	2.3
95% CI								1.6-3.2	1.2-4.6

[1]Baseline exposure category. Risks of lung cancer for this category relative to non-tobacco users were: 1-29 years of use, 3.3 (males) and 1.9 (females): and 1-9 cigarettes per day, 2.0 (males) and 1.0 (females). – [2]Test of linear trend within cigarette type cytegory, $p < 0.001$.

the proportion of years during which nonfilter brands were consumed.

Smoking intensity factors

Table VIII shows that the risk of lung cancer decreased with years since cessation of smoking and increased with frequency and depth of inhalation after adjustment for duration of use for filter, mixed and nonfilter smokers. There were little or no differences in the gradients by cigarette type. These patterns were similar when further adjustment was made for number of cigarettes smoked per day.

The RRs for frequency and depth of inhalation were cross-classified by years of use and by number per day (Table IX). (Data are for combined cigarette types and are given for males only; results are similar for females, but more variable due to smaller numbers of subjects.) The risks with smoking intensity and years of use appeared to increase independently of each other; there was an approximately 3-fold increase from shortest to longest category of years of use and a 1.5-fold increase for the extreme categories of the intensity variables. This pattern was somewhat different when the inhalation factors were cross-classified with number of

TABLE VI – RELATIVE RISK OF LUNG CANCER BY YEARS OF USE AND NUMBER OF CIGARETTES PER DAY FOR LIFETIME FILTER, NONFILTER AND MIXED USERS. ALL RISKS ADJUSTED FOR YEARS SINCE CESSATION, MALE SMOKERS ONLY

Years of use	Number of cigarettes per day											
	Filter				Mixed				Nonfilter			
	1-9	10-19	20-29	30+	1-9	10-19	20-29	30+	1-9	10-19	20-29	30+
1-29	1.0[1]	3.1	3.7	9.6	1.0[1]	1.0	1.8	1.4	1.0[1]	1.7	2.1	3.2
30-39	5.1	6.7	10.4	30.2	1.4	1.6	2.2	2.7	1.1	3.5	4.3	4.6
40-49	14.0	19.3	17.5	20.5	1.9	1.7	2.6	4.1	0.6	3.5	5.0	7.2
50+	18.6	22.5	66.1	13.4	1.9	2.1	2.8	3.8	1.5	3.3	5.2	11.7

[1]Baseline exposure category. Among 1-9 cigarette per day 1-29 year users and after adjusting for cessation, the risks of mixed and nonfilter use relative to filter use were 3.7 and 3.8, respectively.

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TABLE VII – RELATIVE RISK OF LUNG CANCER BY THE PROPORTION OF YEARS NONFILTER BRANDS WERE USED. ALL RISKS WERE ADJUSTED FOR YEARS OF CIGARETTE USE, NUMBER SMOKED PER DAY AND SINCE CESSATION

Proportion of years nonfilter brands smoked	Males	Females
0.00 (all filter)	1.0[1]	1.0[1]
0.01-0.49[2]	1.5	1.8
0.50-0.69	1.4	1.7
0.70-0.83	1.7	1.9
0.84-0.99	1.7	2.1
1.00 (all nonfilter)	1.7	2.0

[1]Test of linear trend, $p < 0.001$. – [2]Exclusive of 0 and 1, categories are [illegible].

cigarettes smoked per day. The gradient of increased risk with greater frequency and depth of inhalation was greater among those who smoked fewer cigarettes per day. Conversely, the risks with increased number per day had a steeper gradient among less intense smokers.

Tar levels

Current levels of tar were ascertained for all major cigarette brands (past levels generally were not available). The mean cigarette tar value was calculated for each smoker as the average tar value for all brands smoked, weighted by the number of cigarettes smoked per day, *i.e.*,

$$\Sigma_i \text{ (No./day)}_i \times \text{tar}_i / \Sigma_i \text{(No./day)}_i$$

where summations are over all brands smoked. Since cigarette brands varied by country and tar measurements were carried out nationally, tar values were not comparable between countries. Therefore, six categories of cigarette tar level were defined within country by the 10%, 25%, 50%, 75%, and 90% quantiles then adjusted across study center. Keeping in mind the measurement differences, the mean tar values for the countries for each category were 15.6, 18.5, 20.6, 23.6, 25.2 and 29.8 mg. Excluded from the tar analysis were all respondents for whom a complete smoking history could not be obtained or any cigarette tar value was unavailable. Table X shows that the RRs, adjusted for years of use, number smoked per day and years since cessation, increased (although not smoothly) with mean tar value, with no significant difference in the trends by sex.

To examine the effects of years of smoking cigarettes at various tar levels, we ranked the cigarette brands within each country by current tar amounts and categorized them by tertiles into high-, medium- and low-tar brands. The number of years of smoking brands from each category was accumulated for each respondent. Among male smokers the cases averaged 28.8, 5.7 and 3.9 years using the high-, medium- and low-tar brands, respectively, while the corresponding control values were 24.5, 5.7 and 3.8 years. Among female smokers the mean years at successively lower tar levels were 20.7, 10.0 and 5.0 years for cases and 14.2, 10.8 and 5.4 years for controls. Table XI shows that after adjusting for years of cigarette use, number smoked per day and years since cessation, males who smoked the highest tar brands exclusively or for more than 75% of the time had a greater risk of lung cancer than those smoking predominantly the lowest tar brands, while those smoking cigarettes of mixed tar levels were at intermediate risk. Among females the patterns of risk were less consistent owing to small numbers, although the greatest risk occurred among the high-tar smokers exclusively. As can be seen from the Table, the type of cigarettes used differed markedly by sex. While 38.5% of all male users smoked the highest tar brands exclusively, 12.2% of the females did so. Among male smokers 10.9% never used the highest tar brands, compared to 33.0% among females.

DISCUSSION

The results of this large international investigation paralleled several other retrospective (Bross and Gibson, 1968; Dean *et al.*, 1977; Rimington, 1981; Wynder

TABLE VIII – RELATIVE RISK OF LUNG CANCER BY YEARS SINCE CESSATION OF CIGARETTE USE AND FREQUENCY AND DEPTH OF INHALATION. ALL RISK ADJUSTED FOR YEARS OF USE

	Males					Females				
	Cases	Controls	Filter RR	Mixed RR	Nonfilter RR	Cases	Controls	Filter RR	Mixed RR	Nonfilter RR
Years since cessation										
0	71%	60%	1.0[1]	1.0[1]	1.0[1]	80%	72%	1.0[2]	1.0[1]	1.0
1-4	13%	10%	0.9	0.9	1.0	11%	10%	0.8	0.9	1.9
5-9	7%	9%	0.9	0.7	0.5	5%	7%	0.9	0.7	0.9
10+	9%	22%	0.4	0.5	0.3	4%	11%	0.3	0.2	0.4
Frequency of inhalation										
Rarely/never	10%	14%	1.0[1]	1.0[1]	1.0[1]	10%	21%	1.0	1.0[2]	1.0[3]
Part of the time	5%	6%	2.2	1.1	1.6	8%	10%	1.3	2.6	1.6
Most of the time	13%	14%	2.1	1.7	1.7	17%	15%	2.7	3.2	—
All of the time	72%	67%	2.4	1.8	1.6	65%	54%	1.6	3.5	2.7
Depth of inhalation										
Slightly/never	8%	10%	1.0[1]	1.0[1]	1.0[1]	21%	37%	1.0	1.0[3]	1.0[3]
Moderately	31%	31%	1.5	1.3	1.4	36%	39%	1.5	2.2	2.9
Deeply	53%	48%	2.1	1.9	1.7	43%	24%	2.6	4.5	2.5
Total[4]	6,630	10,439				551	567			

[1]Test for linear trend, $p < 0.001$. – [2]Test for linear trend, $p < 0.05$. – [3]Test for linear trend, $p < 0.01$. – [4]Due to incomplete data, the number of respondents varied slightly for each variable.

TABLE IX – RELATIVE RISK OF LUNG CANCER BY YEARS OF CIGARETTE USE, NUMBER PER DAY AND INTENSITY RELATED FACTORS. MALE USERS ONLY

	Years of use				
	1-29	30-39	40-49	50+	Adjusted
Frequency of inhalation					
Rarely/never	1.0[1]	2.2	2.6	3.0	1.0[2]
Part of the time	1.6	2.4	3.3	3.1	1.4
Most of the time	1.3	3.0	3.7	4.6	1.7
All of the time	1.6	3.1	4.1	4.5	1.7
Depth of inhalation					
Slightly/never	1.0[1]	2.2	2.9	3.3	1.0[2]
Moderately	1.4	2.9	4.2	4.3	1.4
Deeply	1.8	3.2	3.8	4.6	1.7
	Number per day				
	1-9	10-19	20-39	40+	Adjusted
Frequency of inhalation					
Rarely/never	1.0[1]	2.5	4.0	5.1	1.0[2]
Part of the time	2.0	2.4	4.0	7.8	1.3
Most of the time	1.7	3.1	5.9	5.9	1.5
All of the time	2.0	3.6	4.9	6.4	1.4
Depth of inhalation					
Slightly/never	1.0[1]	2.5	3.5	4.8	1.0[2]
Moderately	1.6	2.5	4.5	4.6	1.2
Deeply	2.2	3.3	4.3	6.3	1.4

[1] Risk of baseline category for variables among 1-29 year relative to never smoked: frequency 3.1 and depth 3.1; and among 1-9 per day users frequency 3.3 and depth 3.9. – [2] Test of linear trend, $p < 0.001$.

TABLE X – RELATIVE RISK OF LUNG CANCER BY MEAN CIGARETTE TAR CONTENT. ALL RISKS ADJUSTED FOR YEARS OF USE, NUMBER SMOKED PER DAY AND CESSATION

Mean cigarette tar content[1]	Males			Females		
	Cases	Controls	RR	Cases	Controls	RR
I (lowest)	7%	10%	1.0[2]	27%	41%	1.0[2]
II	13%	14%	1.2	18%	14%	1.9
III	21%	16%	1.7	15%	11%	1.3
IV	38%	36%	1.3	28%	24%	1.1
V	16%	17%	1.3	9%	9%	1.5
VI (highest)	5%	7%	1.4	3%	1%	—
Total number	2,650	4,279		313	368	

[1] Categories were the within-country 10, 25, 50, 75 and 90th percentiles. Mean tar values within categories were 15.6, 18.5, 20.6, 23.6, 25.2 and 29.8 mg. – [2] Test of linear trend, $p < 0.01$.

et al., 1970; Wynder and Stellman, 1979) and prospective studies (Hammond *et al.*, 1976), which showed that, although risk of lung cancer was substantially greater among filter smokers than among nonsmokers, smoking filter cigarettes was associated with a smaller lung cancer risk than smoking nonfilter brands. A review by Lee and Garfinkel (1981) of studies addressing this issue indicated that filter smokers have a lung cancer risk which is 75% of the risk for nonfilter smokers. In our study, risks among filter smokers, adjusted for duration, number per day and cessation, were 59% (for males) and 49% (for females) of those of nonfilter smokers. The greater reduction may be due to our ability to define lifetime filter smokers, whereas other studies frequently relied on current or recent cigarette type and risks may have been affected by previous use of nonfilter brands. Because of the large number of respondents, we were able to show that the reduction in risk occurs for both sexes, even after adjustment for duration of use and number of cigarettes smoked per day.

Classification of brands into filter or nonfilter type has been used frequently as a convenient surrogate for cigarette tar exposure. However, due to improved filters and new tobaccos and blends, the amount of tar per cigarette has declined substantially over the years so that current nonfilter cigarettes often have less tar than previous filter brands (Maxwell, 1976; Wynder and Stellman, 1979). This means that epidemiologic investigations based on filter/nonfilter classification or current tar levels must be interpreted cautiously. Four studies have reported a substantial increase in risk with total tar intake (Hammond *et al.*, 1976; Joly *et al.*, 1983; Kunze and Vutuc, 1980; Vutuc and Kunze, 1980), although only Hammond *et al.* (1976) used historical tar values. [Two of these (Kunze and Vutuc, 1980; Vutuc and Kunze, 1980) were based on analyses of subsets of the data reported in this paper]. In this study we ranked each brand within country by tar content; in this way the risks were interpretable historically under the assumption that the *relative* tar ranks are unchanged. Our data showed that long-term smokers of the lowest tar brands were at about two-thirds of the cancer risk compared to long-term smokers of the highest tar brands. In these data the highest tar brands delivered about twice as much tar as the lowest brands, so that additional reductions can be expected with current low-tar brands, some of which contain less than one-fifth the levels of the highest tar brands.

Many reports have linked increased lung cancer risk with increased duration of cigarette use, number smoked per day and frequency and depth of inhalation [see the Surgeon General's Report (USPHS, 1982) for a review and references]. Few, however, have consid-

TABLE XI – RELATIVE RISK OF LUNG CANCER BY THE PROPORTION OF YEARS HIGH-, MEDIUM- AND LOW-TAR BRANDS WERE USED. ALL RISKS WERE ADJUSTED FOR YEARS OF CIGARETTE USE, NUMBER SMOKED PER DAY AND YEARS SINCE CESSATION

Proportion of smoking history[1]	Males			Females		
	Cases	Controls	RR	Cases	Controls	RR
Low-tar brands (100%)	3%	5%	1.0	5%	13%	1.0
Low-tar brands (>75%)	1%	1%	1.2	1%	3%	—
Other mixed levels	24%	40%	1.5	60%	58%	5.9
High-tar brands (>75%)	20%	15%	1.8	19%	16%	4.0
High-tar brands (100%)	38%	39%	1.7	14%	10%	7.7
Total number	2,650	4,279		313	368	

[1] Tar brand categories were less than 16.4 mg (low) and 19.2 mg or more (high).

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ised the combined effects of these factors. Our data indicate that the deleterious effects of duration of use and number per day appeared to act multiplicatively, and the higher risk with nonfilter compared to filter use remained after adjusting for duration, number per day and cessation. The patterns of relative risks for frequency and depth of inhalation were similar within categories of duration but varied by number per day. In line with Doll and Peto (1976), who reported an effect of inhalation limited to light (less than 25 cigarettes per day) smokers, we found the increased risk associated with deep inhalation was greatest among those smoking the smallest number per day (although some excess was found in all inhalation groups).

Sources of possible bias needed to be considered in this study, since the multicenter design encompassing five European countries made some differences in survey methods unavoidable. The methods of case acquisition were similar among centers, with nearly all lung cancer cases admitted to the designated hospitals being included in the study. However, at several centers the location of the case within the hospital precluded interviewer blindness. Indeed, at two study sites specialized hospitals were utilized for case acquisition with controls obtained from a different hospital. Three points, however, argued against the interviewer's knowledge of patient status seriously influencing data collection: (1) the questions were of a closed form so that little interviewer discretion was possible; (2) being aware of this potential problem, interviewers were carefully instructed to avoid influencing patient response; and (3) the patterns of risks observed were similar between those centers where interviewers were blind to patient status and centers where they were not blind.

The differences in control selection procedures in this hospital-based study is of concern. Controls were hospital-matched, except as noted above, but there were differing distributions of admission diagnoses from center to center. All centers excluded as potential controls persons admitted for tobacco-related disorders. During the initial phase of the study, controls (but not cases) were restricted further to exclude those with a *history* of tobacco-related diseases, a procedure likely to result in an upward bias in the relative risk estimates, since tobacco use among those controls was likely to be low. This procedure was discontinued after 6 months at all but the French center. (The Rome segment of the study was initiated 1 year after the others, so that this additional control restriction was never implemented.) The change in the acceptable control criteria had no measurable effect on the risk estimates, however, due to the relatively small number of subjects enrolled during this start-up phase. (The RRs from the French data were elevated, but still within the range of all centers and showed similar trends to those seen elsewhere.) An additional concern of the control selection related to differences in the referral area for cases and controls, since cases may have been derived from a wider geographic area. Thus male cases were more likely to have been born or spent their childhood, teen or adult years in a rural environment. The RRs associated with residential history were small, with a maximum matched RR for rural vs. urban environment of 1.3, so that confounding by this factor did not seriously affect the RRs associated with the smoking variables. No residential differences were observed for females.

A problem in studies of well-publicized health associations, such as smoking and lung cancer, is recall bias, with cases more likely to remember cigarette exposure. This was not thought to be a major problem since the level of the awareness of the health issues surrounding smoking was high among both cases and controls. At the start of the interview, respondents were informed only that the survey was to gather general health information. In addition, the questionnaire was designed to assist recall by systematically moving from the most recent cigarette brand to the earliest. In any case, there would be no expectation that recall differences would occur for brand names, from which tar value and filter/nonfilter status were obtained. Further, although lung cancer patients may have been aware of some respiratory problems, it was not general medical procedure in these study areas to inform patients of their diagnosis.

In this report RRs were presented adjusted for study center. In general the risk patterns were similar for each center, differing at times only in the level of RR. A detailed evaluation of RRs by center is beyond the scope of this paper.

In summary, this case-control study, the largest of its kind, allowed detailed analysis of the relative effects of smoking filter and nonfilter cigarettes. Our findings indicate that lifetime filter smokers have a lower risk relative to lifetime nonfilter smokers than previously thought. Still, lifetime filter smokers are at a substantially higher risk of lung cancer compared to those who never smoked. For both filter and nonfilter smokers, risks increased with the intensity and duration of use. These findings indicate that smoking cessation must be the primary goal of efforts to prevent lung cancer, although changing to low tar (filter) cigarettes should help in reducing risk.

ACKNOWLEDGEMENTS

This study was carried out under contracts from the Office of Smoking and Health of the National Cancer Institute. Enviro Control, Inc. was the prime contractor for the initial 4½ years of data collection, with the Environmental Epidemiology Branch of the NCI monitoring the study for the remaining 6 months. We wish to thank Drs. G. Gori, D. Luecke and T. Owen of the NCI and Dr. C. Lynch and Ms. D. Potter of Enviro Control for their efforts in operation of the study and for facilitating transfer of the data to the NCI. We also thank Drs. J. Fraumeni, Jr., R. Hoover, E. Benhamou, E. Riboli and C. Vutuc and Mr. D. Hole for advice and assistance with these analyses, as well as Ms. Kandy Krump of ORI, Inc. and Mr. Peter Lee of the NCI for programming support.

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Int. J. Cancer: 33,

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